

69. (New) Use of isolated adrenomedullin peptide PAMP-20 (SEQ ID NO: 7) or antibodies reactive therewith for promoting organ and bone development.
70. (New) An isolated adrenomedullin oligonucleotide selected from the group consisting of AM₉₄₋₁₁₄ (SEQ ID NO: 4), AM₄₄₄₋₄₆₄ (SEQ ID NO: 5) and AM₂₈₉₋₃₀₉ (SEQ ID NO: 6).

REMARKS

In this Preliminary Amendment, pages 3, 8, 12, 13 and 15 of the specification have been amended. A marked up copy of the replacement/rewritten paragraphs of the specification as specified above is provided herewith on pages 10-12. The line numbers herein refer to the line numbers of the published PCT application no. WO 97/07214 (PCT/US96/13286). Claims 1-43 have been canceled without prejudice; new claims 44-70 have been added to remove redundancies among the claims in the parent application. The new claims are fully supported by the previous claims.

AUTHORIZATION

Should any additional fees be deemed to be properly assessable in this application, the Commissioner is hereby authorized to charge Deposit Account No. 13-4500, Order No. 2026-4202US4. **A duplicate copy of this sheet is attached.**

Respectfully submitted,

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Replacement Paragraphs of the Specification – Marked up Copy

Please amend the specification by replacing/rewriting the paragraphs as indicated.

At page 3, please replace/rewrite paragraph 2 from lines 16-35, as follows:

(Amended)

AM's role as a vasodilatory agent has been extensively studied (C. Nuki et al., Biochem. Biophys. Res. Commun. 196, 245 (1993); Q. Hao et al., Life Sci. 54, 265 (1994); D. Y. Cheng et al., Life Sci., 55, 251 (1994); C. J. Feng, B. Kang, A. D. Kaye, P. J. Kadowitz, B. D. Nossaman, Life Sci., 433 (1994)). It acts through specific receptors in the plasma membrane to activate adenylate cyclase activity and modulate Ca^{2+} flux in the target cells (S. Eguchi et al., Endocrinology 135, 2454 (1994); Y. Shimekake et al., J. Biol. Chem. 270, 4412 (1995)). These signal transduction pathways are involved in numerous physiological processes, including the regulation of hormone secretion. It is well established that regulation of intracellular cAMP modulates hormone release in the pancreas (Y. Korman, S. J. Bhathena, N. R. Voyles, H. K. Oie, L. Recant, Diabetes 34, 717 (1985); C. B. Wollheim, Diabetes 29, 74 (1980)). AM has also been reported to have an effect on Na^+ channel activity (EP Application No. 0 622 458 A2). Since AM has been reported to influence the secretion rate of several hormones, including catecholamine (F. Kato et al., J. Neurochem. 64, 459 (1995); EP Application No. 0 622 458 A2), adrenocorticotropin (W. K.

At page 8, please replace/rewrite paragraph 2 describing "Figure 8", from lines 16-24, as follows:

(Amended)

Figures 8A and 8B [Figure 8]: Characterization of AM by RT-PCR in mRNA from normal tissues and pulmonary tumor cell lines. The PCR products had the proper size (410bp) when visualized with UV light (Figure 8B) [(lower panel)], and they hybridized with the specific probe after Southern blot (Figure 8A) [(upper panel)]. H146 and H345 are small cell carcinomas, H676 is an adenocarcinoma, H720 is a carcinoid, and H820 is a bronchioalveolar carcinoma. H146 was the only cell line that tested negative for AM.

At page 12, please replace/rewrite paragraph 3 from lines 6-10 as follows:

(Amended)

Figures 25A and 25B [Figure 25]: Figures 25A and 25B [Figure 25] set forth the distribution of amphipathic regions for AM and PAMP as calculated for a-helix/b-sheet angle parameters (Eisenberg), and the helical wheel projection display for AM and PAMP (DNASTAR).

At page 12, please replace/rewrite paragraph 6 from lines 34-35 as

follows:

(Amended)

Figures 28A-28D [Figures 28A and 28B]: Figures 28A-28D set [Figure 28 sets] forth the growth effects of AM. A representative human tumor cell line,

At page 13, please replace/rewrite paragraph 2 under "DETAILED DESCRIPTION OF THE INVENTION" from lines 18-19, as follows:

(Amended)

Specifically, the present invention relates to the following novel isolated AM peptide and oligonucleotide sequences [peptides]:

At page 15, please replace/rewrite paragraph 3, lines 30, as follows:

(Amended)

To characterize the functions of AM in normal tissues, the distribution of AM was studied in normal and malignant lung using immunocytochemical techniques to localize the peptide, and [in] *in situ* reverse transcriptase-polymerase chain reaction (RT-PCR) to study the expression of its messenger RNA (mRNA) in formalin-fixed paraffin-embedded specimens.